□ CASE REPORT □

Brain Metastasis in Malignant Pleural Mesothelioma

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A 55-year-old male who had a remote history of occupational asbestos exposure consulted us because of chest pain. Chest X-ray revealed diffuse pleural thickening and pleural effusion on the right. A diagnosis of malignant mesothelioma, biphasic type was made by needle pleural biopsy. Fourteen months later, the patient died of brain metastasis. At autopsy, malignant mesothelioma of the pleura with metastasis to the brain and bilateral adrenal glands was observed. Brain metastases proven by autopsy are rare in cases of malignant mesothelioma. The ferruginous body count in the lung tissue was 16 per gram of wet weight.
(Internal Medicine 36: 591–594, 1997)

Key words: asbestos-related pulmonary disease, the syndrome of inappropriate secretion of antidiuretic hormone, ferruginous body, pleural disease

Introduction

Brain metastasis in malignant mesothelioma is rare (1). In the present case, we made an antemortem diagnosis of brain metastasis from pleural mesothelioma by pleural biopsy and brain computed tomography (CT), which was later confirmed by autopsy. We also tried but failed to confirm the occupational asbestos exposure by demonstrating asbestos bodies in the postmortem lung. Although the number of reports of brain metastasis in malignant mesothelioma is increasing, we found only 18 cases proven by autopsy (2–13).

Case Report

The patient was a 55-year-old male who had worked in a factory, where he had been fixing jute bags for recycling use from the age of 20 to 23 years old. Many of those jute bags were used to carry imported asbestos. The patient had been well until August 1994 when he first noted nonproductive cough. He consulted a chest physician who diagnosed pleuritis of unknown etiology, and treated him with pleurodesis and antituberculosis regimen without benefit. As there was continuing dull pain in his right hemi-thorax, he was referred to Kinki University Hospital for further examination. Chest X-ray (Fig. 1) and CT scan (Fig. 2) revealed diffuse pleural thickening and pleural effusion on the right. A diagnosis of malignant pleural mesothelioma was made by needle biopsy. Histological variants included tubular, gland-like, and sarcomatous patterns. Tubular and gland-like structures were formed by cuboidal or taller cells (Fig. 3a). Hyaluronic acid was detected on the luminal surface of these cells. Sarcomatous areas were composed of spindle cells organizing poorly formed bundles (Fig. 3b). Since there was a mixture of epithelial and sarcomatous components, the diagnosis of biphasic malignant mesothelioma was made.

In December 1995, he was readmitted because of increasing dyspnea. Chest X-ray showed increased size of the pleural mass and no pneumonic infiltrate. On the third hospital day, he was disoriented and became unconscious. Lumbar puncture showed clear spinal fluid with normal pressure. Cytology, protein, sugar and other chemical measurements of the fluid were negative. A brain CT (Fig. 4) revealed two high absorption areas circumscribed by edematous lesions in the right frontal lobe and caudate nucleus. A tentative diagnosis of brain metastasis of malignant pleural mesothelioma was made. Intravenous glycerol injection resulted in temporary relief, and the patient developed disseminated intravascular coagulation (DIC). On December 28, serum and urine sodium levels were 116 and 109 mEq/*l*, respectively, and the urine osmolarity was 313 mOsm/*l*. A clinical diagnosis of the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) was made and was treated with water restriction and infusion of hypertonic saline. The patient died after a month of the treatment.

At autopsy, malignant mesothelioma involving the right pleura with shallow invasion of the lung parenchyma, thoracic wall and diaphragm, with metastasis to the brain and bilateral

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Received for publication November 21, 1996; Accepted for publication April 21, 1997
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adrenal glands was found. Round and hemorrhagic lesions of 1 to 2 cm in diameter were found in the left superior frontal gyrus, right inferior frontal gyrus, right caudate nucleus and left temporal lobe. Hypothalamus was not involved. All brain and adrenal lesions were histologically the same as the primary mesothelioma, although the sarcomatous component was more prominent (Fig. 3c). The left lung revealed bronchopneumonia in the lower lobe. Ferruginous body count was 16 bodies per gram of wet pulmonary tissue by the method of Smith and Naylor (14).

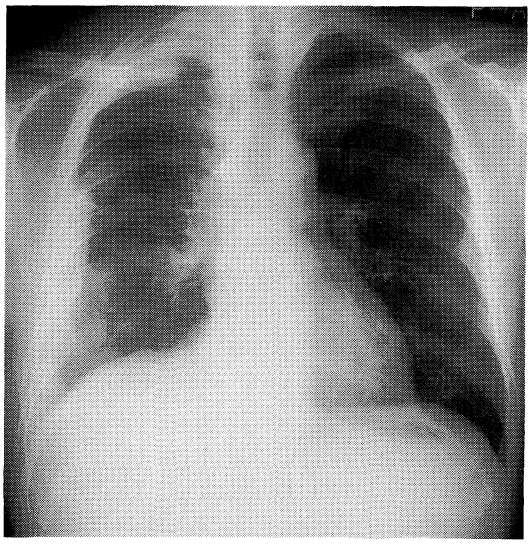

Figure 1. Chest X-ray on admission showing diffuse pleural thickening on the right.

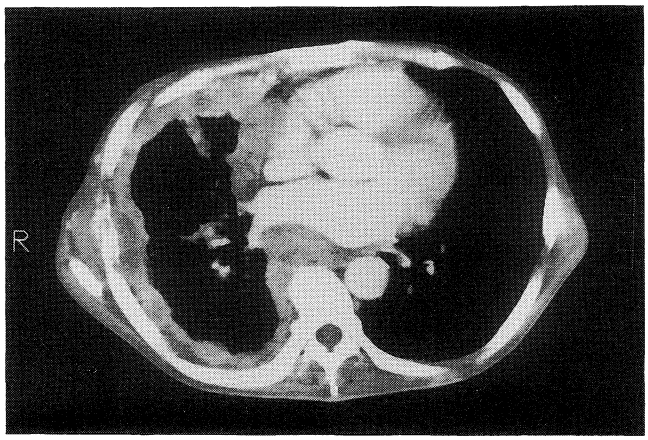

Figure 2. Chest CT on admission showing diffuse pleural thickening on the right.

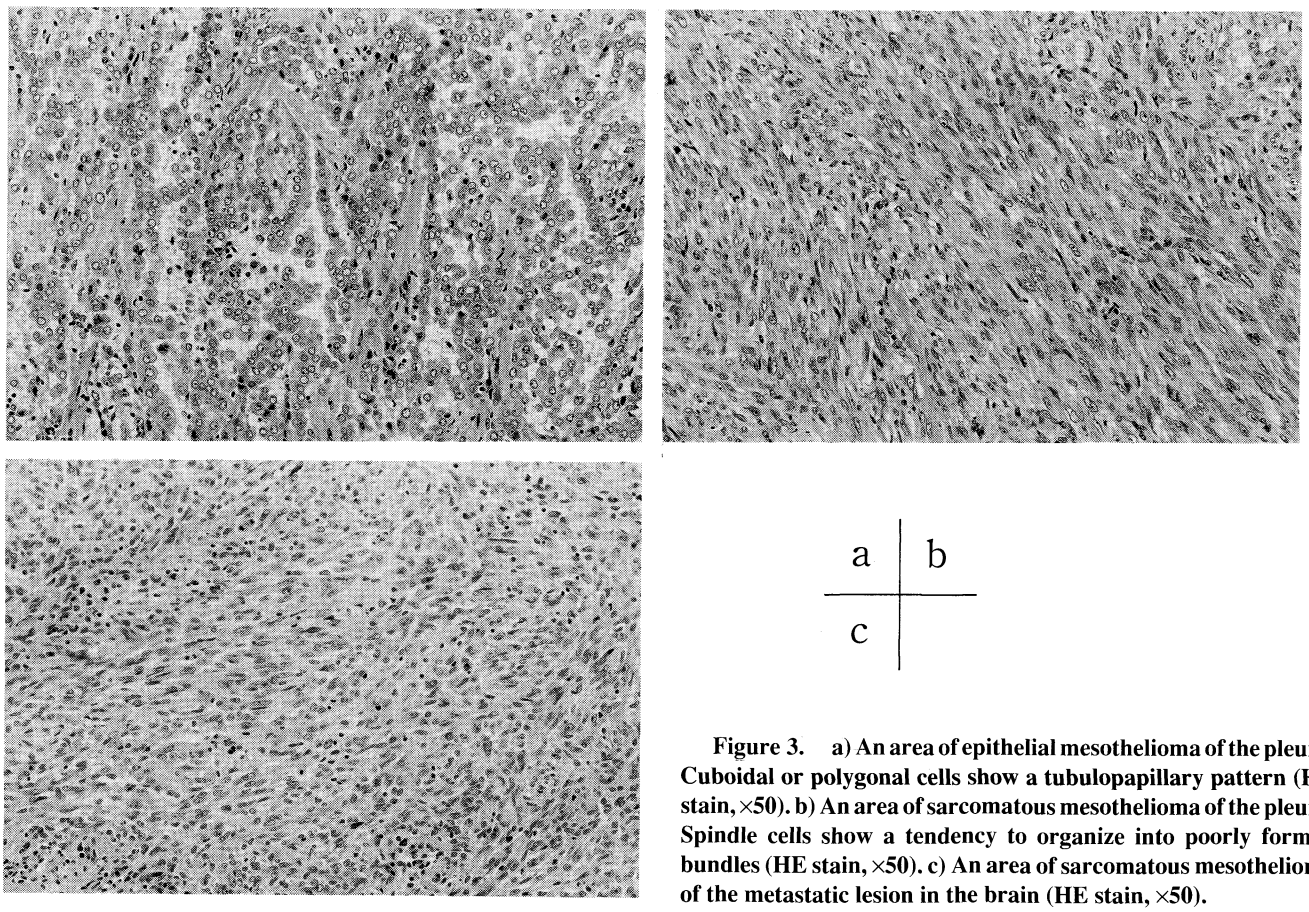

Figure 3. a) An area of epithelial mesothelioma of the pleura. Cuboidal or polygonal cells show a tubulopapillary pattern (HE stain, ×50). b) An area of sarcomatous mesothelioma of the pleura. Spindle cells show a tendency to organize into poorly formed bundles (HE stain, ×50). c) An area of sarcomatous mesothelioma of the metastatic lesion in the brain (HE stain, ×50).

Discussion

In addition to benign pleural diseases including pleural plaques, mesothelioma, asbestosis and lung cancer are the most frequent occupational lung diseases in workers exposed to asbestos dust (15). Although malignant mesothelioma is no longer a rare disease, its brain metastases are rare. Wronski and Burt (11) reviewed the case reports of brain metastases in pleural mesothelioma and divided the total 54 cases into three categories, i.e., proven by neuropathology (15 cases), "unproven" autopsy or clinical (9 cases), and "mentioned" autopsy or clinical (30 cases). Unproven cases included patients with malignant mesothelioma whose brain metastases were diagnosed clinically by brain CT scan (4 patients) or found during autopsy (5 patients), but not clearly documented by autopsy. For 30 cases of the third category, each author only mentioned the findings within the table of their article.

Figure 4. CT of the brain showing enhanced masses in the right frontal lobe and caudate nucleus.

In our computer-assisted search (MEDLINE 1966–1996 and JMEDLINE 1981–1996) for literature of brain metastases in malignant mesothelioma, we found three additional cases of the proven category (7, 12, 13). Thus, a total of 19 proven cases of brain metastases in malignant mesothelioma, including the present case have been reported. Within the list of "proven cases" reported by Wronski and Burt (11), we were not able to access the report of Bianchi and colleagues (16) and the details of two cases were not mentioned in the report of Henderson and colleagues (17). Thus, we excluded those three cases and the summary of 16 proven cases of brain or dural metastasis of malignant mesothelioma are tabulated in Table 1.

In sixteen proven cases with brain or dural (11) metastasis of malignant mesothelioma, the primary sites were all pleura, except for one pericardium (8). Most of the cases were male (88%) and were older than 45 years. The left and right sides were equally affected. Histological typing of the cases with brain metastasis revealed that the sarcomatous type predominated (75%) (Table 1). In the present case, the metastatic lesions to the brain showed a sarcomatous pattern, although the primary tumor was biphasic. Therefore it may be assumed that sarcomatous histology is more likely to metastasize to the brain. Among these cases, extracranial metastases were to the lung (44%), liver (38%), mesentery or omentum (31%), adrenals (31%) and bone (19%) (Table 1). In three cases, the brain was the only site of metastasis. A positive history of occupational asbestos exposure was reported in 92% of the cases. In the present case, the ferruginous body count did not indicate a sufficient number of asbestos fiber deposits in the lung to assess the occupational exposure (18) though a possible history was present.

The complication of SIADH among the patients with mes-

Table 1. Reported Cases of Malignant Pleural Mesothelioma with Autopsy Proven Intracranial Metastasis

Author (Reference number)	Year	Age	Sex	Primary site	Histological type	Extracranial metastasis	Asbestos exposure
Grumme and Bingas (2)	1973	49	F	Right pleura	Sarcomatous	Lung	ns*
Grumme and Bingas (2)	1973	46	F	Left pleura	Sarcomatous	Lung, ileum	ns
Walters and Martinez (3)	1975	52	M	Left pleura	Epitheloid	Lung, liver, diaphragm	Present
Schwechheimer and Butzengeiger (4)	1983	70	M	Left pleura	Sarcomatous	Diaphragm, nodes, chest wall, adrenals	Present
Harrison (5)	1984	45	M	Right pleura	Sarcomatous	Lung, liver, ometum, adrenals	Present
Kaye et al (6)	1986	48	M	Right pleura	Sarcomatous	Vertebrae, mesentery, right atrium, liver	Present
Satoh et al (7)	1987	78	M	Left pleura	Sarcomatous	Jejunum, mesenteric nodes, adrenals	Present
Asoh et al (8)	1990	50	M	Pericardium	Epitheloid	Lung	ns
McNaughton et al (9)	1990	63	M	Right pleura	Sarcomatous	None other than brain	Present
Falconieri et al (10)	1991	69	M	Left pleura	Sarcomatous	Lung, vertebrae, mesentery, right atrium, liver	Present
Falconieri et al (10)	1991	64	M	Left pleura	Sarcomatous	Lung, stomach, pericardium, adrenals, kidney, thyroid	Present
Falconieri et al (10)	1991	79	M	Right pleura	Sarcomatous	Vertebrae, mesentery, right atrium, liver	Present
Wronski and Burt (11)	1993	52	M	Left pleura	Biphasic	None other than brain	Absent
Sato et al (12)	1994	65	M	Left pleura	Sarcomatous	Dura, lung, hilum, liver, bone	Present
Kitai et al (13)	1995	62	M	Right pleura	Sarcomatous	None other than brain	Present
Present case	1996	55	M	Right pleura	Biphasic	Adrenals	Present

othelioma is rare and only two cases have been reported (19–20). On the other hand, SIADH is not a rare complication of brain tumors. We assumed that the possible complication of SIADH in the terminal stage of this case was a consequence of brain metastasis of malignant mesothelioma.

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